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KIM, JENNIFER M	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,233	CINCOTTA, ANTHONY H.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/8/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-11 are presented for Examination.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 2, 4 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the simultaneously treating hypertension, hypertriglyceridemia, a proinflammatory state, and insulin resistance associated with Metabolic Syndrome comprising administering a **"specific" central acting dopamine agonist (i.e. bromocriptine)**, does not reasonably provide enablement for the simultaneously treating hypertension, hypertriglyceridemia, a proinflammatory state, and insulin resistance associated with Metabolic Syndrome comprising administering **a "central acting dopamine agonist"**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method of simultaneously treating hypertension, hypertriglyceridemia, a proinflammatory state, and insulin resistance associated with Metabolic Syndrome comprising administering **a "central acting dopamine agonist"**. The nature of the invention is extremely complex in that it encompasses the actual treatment of various disease symptoms of a Metabolic Syndrome such that the subject treated with above compounds simultaneously treat the various symptoms.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass simultaneous treatment of various symptoms of metabolic syndrome in humans which has potentially many different causes (i.e. many different mutations or combination of mutations). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed **any "central acting dopamine agonist"** to a subject in order to actually treat all the symptoms is minimal. All of

the guidance provided by the specification is directed towards **a single, specific compound (i.e. bromocriptine)** rather than **any "central acting dopamine agonist"**.

Working Examples: All of the **working examples** provided by the specification are directed toward directed towards the employment of **a single, specific compound (i.e. bromocriptine)** rather than **any "central acting dopamine agonist"**.

State of the Art: While the state of the art is relatively high with regard to treatment of Metabolic syndrome with a specific compound (i.e. bromocriptine), the state of the art with regard to treatment of Metabolic syndrome with **any "central acting dopamine agonist"** is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein **any compound having "central acting dopamine agonist" activity** was administered to a subject to simultaneously treat various symptoms related to metabolic syndrome. The State of the Art, Johnson et al. (U.S.Patent No. 6,342,246 B2) discloses that the apomorphine (central acting dopamine agonist) is usually accompanied by **serious undesirable side effects** such as **hypertension**. (column 1, lines 40-45). Therefore, to the extent that the instant claims are drawn to utilization of **any "central acting dopamine agonist" for simultaneously treating various symptoms including hypertension**, Which is highly speculative, a greater amount of evidence is required to show its operability in humans.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual simultaneous treatment of various symptoms of metabolic syndrome with claimed **any "central acting dopamine agonist"** in a human subject makes practicing the claimed invention unpredictable in terms of the employment of **any "central acting dopamine agonist"**.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed **any "central acting dopamine agonist"** and test the combination in the model system to determine whether or not the combination is effective for simultaneous treatment of various symptoms of metabolic syndrome. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard to employment of **any "central acting dopamine agonist"** for simultaneously treating various symptoms related to metabolic syndrome, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding the employment of **any "central acting dopamine agonist"** for simultaneously treating various

symptom of metabolic syndrome, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention simultaneously treating various symptoms of metabolic syndrome in a subject by administration of one of the claimed **any "central acting dopamine agonist"**.

Therefore, a method a method of simultaneously treating hypertension, hypertriglyceridemia, a proinflammatory state, and insulin resistance associated with Metabolic Syndrome comprising administering **a "central acting dopamine agonist"** is not considered to be enabled by the instant specification.

Written Description

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-11 are drawn to a method of simultaneously treating hypertension, hypertriglyceridemia, **a proinflammatory state**, and insulin resistance associated with Metabolic Syndrome comprising administering a central acting dopamine agonist. The claims thus encompass a broad genus of a proinflammatory state. The instant specification does not describe or exemplify any proinflammatory state. This instant specification therefore does not provide a basis for one of skill in the art to envision the inflammation state involving cytokines, chemokines, adhesion molecules, transcription

factors and proteases associated with metabolic syndrome. The instant specification does not describe or exemplify any pro-inflammatory state. This instant specification, therefore, does not provide a basis for one of skill in the art to envision such pro-inflammatory state associated with metabolic syndrome. Therefore, given the broad genus of a proinflammatory state encompassed by the rejected claims, and given the lack of a basis provided by instant specification or prior art to envision any pro-inflammatory state associated with metabolic syndrome that are necessary capable of inducing various symptoms associated with metabolic syndrome, one of skill in the art would not have been able to envision a sufficient number of proinflammatory state/factors associated with metabolic syndrome to describe broadly claimed genus. Therefore, one of skill in the art would reasonably have concluded Applicants' were not in possession of the claimed invention of a pro-inflammatory state.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "pro-inflammatory state" is vague and indefinite because it is not clear what would be the state that would qualify as "pro-inflammatory state" associated with metabolic syndrome without clear definition or the examples of such. One of ordinary skill in the art could not ascertain among a

numerous cytokines, chemokines, transcription factors, which would be qualify to determine such "pro-inflammatory state".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-4, 6-8, 10 and 11 are rejected under 35 U.S.C.102 (a) as being anticipated by Pijl et al. (2002).

Pijl et al. teach that bromocriptine favorably affects various components of the metabolic syndrome simultaneously to ameliorate cardiovascular risk in type 2 diabetes mellitus and it reduces fasting and postprandial serum triglyceride and free fatty acid levels and diminish fasting cholesterol concentrations. Pijl et al. also teach that bromocriptine lowers blood pressure in both humans and animals with hypertension via its sympatholytic capacities. (page 76 under conclusions). Pijl et al. teach that that the data on reduced dopamine neuronal activities in obese animal models of the metabolic syndrome, the indirect evidences of impaired dopaminergic neurotransmission in patients with obesity and the consistently observed markedly beneficial effects of dopaminergic drugs on metabolism in insulin resistant rodents hold great promise for the use of dopaminergic drugs in the treatment of patients with type 2 diabetes mellitus and that a quick release form of bromocriptine, Ergoset (1.5 to 2.5mg/day orally) is by

far the most (if not the only) studies compound within this context. (page 74 under 3.Effects of Dopaminergic Drugs on Metabolism in Humans).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 5 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pijl et al. (2002) as applied to claims 1-4, 6-8, 10 and 11 above, and further in view of Cincotta et al. (U.S.Patent No. 5,679,685).

Pijl et al's teaching as applied as before.

Pijl et al. do not teach the specific carriers set forth in claims 5 and 9.

Cincotta et al. teach and illustrate a composition comprising bromocriptine formulated with carriers such as lactose, starch and magnesium stearate. (column 4 lines 10-20).

It would have been obvious to one of ordinary skill in the art to modify bromocriptine composition taught by Pijl et al. and formulated with the carriers that are known to be compatible with bromocriptine in a pharmaceutical formulation including lactose, starch and magnesium stearate. One would have been motivated to make such a modification because Cincotta et al. teach the formulation comprising bromocriptine is preferably combined with the carriers such as lactose, starch and magnesium stearate as illustrated by Cincotta et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-11 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-11 of copending Application No. 10/944,631. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-46 of copending Application No. 10/944,631. Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass the same subject matter of treating the symptoms associated with Metabolic Syndrome. As such, the

claims of the instant Application and the patented claims would have been obvious variations of the other to one of ordinary skill in the art and would obviously be treated upon the treatment of the same underline cause of Metabolic Syndrome.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
March 21, 2008